

**TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371**

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

09/14/237

INTERNATIONAL APPLICATION NO.

PCT/JP98/01094

INTERNATIONAL FILING DATE

March 16, 1998

PRIORITY DATE CLAIMED

March 21, 1997

TITLE OF INVENTION

Immunopotentiators

APPLICANT(S) FOR DO/EO/US Eiichiro YAGI, Masako NAGANUMA, Ichiro IWAI,
Masato HATAO, Kenji YAMAGUCHI and Genji WADA

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☒ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☒ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information: Claim For Priority

17. ☐ The following fees are:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **\$1070.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **\$930.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **\$790.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **\$720.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **\$98.00**

ENTER APPROPRIATE BASIC FEE AMOUNT =

\$ 1070.00

Surcharge of **\$130.00** for furnishing the oath or declaration later than ☒ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).

\$ 130.00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$
Total claims	14 - 20 =	- 0 -	x \$22.00	\$
Independent claims	14 - 3 =	11	x \$82.00	\$ 902.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$270.00	\$

TOTAL OF ABOVE CALCULATIONS = \$ 2102.00

Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28). +

\$

SUBTOTAL = \$ 2102.00

Processing fee of **\$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).

\$

TOTAL NATIONAL FEE = \$ 2102.00

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **\$40.00** per property +

\$

TOTAL FEES ENCLOSED = \$ 2102.00

Amount to be refunded: \$

charged: \$

a. ☒ A check in the amount of \$ 2102.00 to cover the above fees is enclosed.

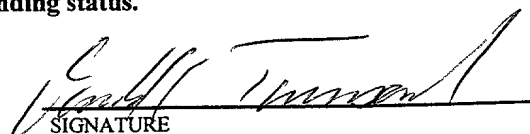
b. ☐ Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 20-1424 A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

TOWNSEND & BANTA
1225 Eye St., N.W.
Suite 500
Washington, D.C. 20005


SIGNATURE

Donald E. Townsend
NAME

22,069
REGISTRATION NUMBER

SPECIFICATION

IMMUNOPOTENTIATORS

5 FIELD OF THE INVENTION

660240-2224160
The present invention relates to a skin immunopotentiator or an endermic liniment against ultraviolet light-induced skin immunosuppression for preventing skin immunosuppression due to exposure to ultraviolet light by external application.

BACKGROUND OF THE INVENTION

15 Skin is an organ which is located in the outermost layer of a living body and it also is an organ which incurs physical, chemical and biological invasion most intensely and directly. Recently it has become clear that the skin is also the most well developed immune organ.

20 The skin consists of corneum cells of the epidermis, Langerhans' cells, dendritic cells of the corium, vascular endothelial cells, macrophages, etc. The Langerhans' cells are believed to play a central role in skin immune function by their ability to process and present antibodies. It is believed that
25 they promptly contact and deal with an antigen which

has entered from the outside as a foreign entity and then move to lymph glands and present the antigen to the T cells, initiating a subsequent series of immune response reactions.

5 Recently, the possibility of ultraviolet light promoting carcinogenesis through a reduction in the skin immune reaction due to ultraviolet light, in addition to the carcinogenic properties of ultraviolet light itself, has been pointed out. It is quite
10 important for the purposes of preventing carcinogenesis due to ultraviolet light to protect against ultraviolet light using anti-sun exposure cosmetics such as sunscreens. However, even during seasons when sunscreens are not used on a daily basis,
15 the immune suppression actions may take place and there is also a concern about various adverse effects other than carcinogenesis on living bodies.

It is also known that, just as the skin immune functions are reduced by aging, various other causes
20 in addition to ultraviolet light reduce the skin immune functions.

Because of the aforementioned reasons, there has been an urgent need to develop drugs with immunopotentiating actions or anti-
25 immunosuppression functions which can be used on a

daily basis.

However, a detailed investigation of the relationships between the various forms of skin immusuppresion due to different causes has not been
5 conducted. For example, there is no guarantee that a substance which controls the skin immunosuppression due to aging can control the skin immunosuppression due to other causes.

Also, there has not been enough research about
10 the prevention of skin immunosuppression due to ultraviolet light compared with research about skin immunosuppression due to aging.

For example, glutathione is known to be administered orally as a substance which controls the
15 skin immunosuppression due to aging (refer to Fragrance Journal No. 82, 1987, p65). However, there has been no research about whether or not the external application of glutathione can control the skin immunosuppression due to aging or whether or
20 not it can control the skin immunosuppression due to ultraviolet light.

The inventors investigated various substances for their effect on preventing the immunosuppressive actions of ultraviolet light and as a result discovered
25 that glutathione, which, when administered orally,

has an effect of preventing immunosuppression due to aging, can also prevent immunosuppression due to ultraviolet light when applied externally. The present invention was completed based on this
5 discovery.

There has been no report on externally applied glutathione regarding its immunopotentiating actions or its effects of alleviating/preventing immunosuppression when used for controlling
10 immunosuppression due to ultraviolet light. The present invention was completed by the discovery to the effect that glutathione can very distinctively, through external application, alleviate/prevent a reduction in immune functions due to ultraviolet light,
15 a discovery which could not have been foreseen by the present party.

For Scutellaria root extract, it has been known that Baicalein, one of its ingredients, has cell potentiating actions (refer to Japanese unexamined
20 patent publication Tokkai Sho 64-50877). However, there has been no research on whether it can control the skin immunosuppression due to ultraviolet light.

The inventors investigated various substances for their effect on preventing the skin
25 immunosuppressive actions of ultraviolet light and as

a result discovered that Scutellaria root extract can prevent immunosuppression due to ultraviolet light. The present invention was completed based on this discovery.

5 There has been no report on Scutellaria root extract regarding its immunopotentiating actions or its effects of alleviating/preventing immunosuppression when used for controlling immunosuppression due to ultraviolet light. The
10 present invention was completed by the discovery to the effect that Scutellaria root extract can very distinctively alleviate/prevent a reduction in immune functions due to ultraviolet light, a discovery which could not have been foreseen by the present party.

15 For linden extract, clove extract, Geranium herb extract and rosemary extract, there has been no research regarding whether they can control the reduction of the immune functions.

20 For the purpose of solving this problem, the inventors investigated various substances for the effect of their on preventing immunosuppressive actions and as a result discovered that linden extract, clove extract, Geranium herb extract and rosemary extract had distinctive immunopotentiating actions as
25 well as the effects of alleviating and preventing a

reduction in immune functions, thus completing the present invention.

There has been no report about the immunopotentiating actions and the
5 alleviation/prevention of immunosuppression by linden extract, clove extract, Geranium herb extract and rosemary extract. The present invention was completed by the new discovery to the effect that linden extract has immunopotentiating actions and
10 alleviates/prevents the reduction of the immune functions due to ultraviolet light.

DISCLOSURE OF THE INVENTION

The present invention provides an
15 immunopotentiator for preventing ultraviolet light-induced skin immunosuppression which characteristically contains glutathione.

Also, the present invention provides a drug
20 against ultraviolet light-induced skin immunosuppression which characteristically contains glutathione.

Furthermore, the present invention provides an immunopotentiating endermic liniment for preventing ultraviolet light-induced skin immunosuppression.

25 Also, the present invention provides an

endermic liniment against ultraviolet light-induced skin immunosuppression which characteristically contains glutathione.

Furthermore, the present invention provides an
5 immunopotentiator for preventing ultraviolet light-induced skin immunosuppression which characteristically contains Scutellaria root extract.

Also, the present invention provides a drug
10 against ultraviolet light-induced skin immunosuppression which characteristically contains Scutellaria root extract.

Furthermore, the present invention provides an immunopotentiator which characteristically contains linden extract.

Also, the present invention provides a drug
15 against immunosuppression which characteristically contains linden extract.

Furthermore, the present invention provides an immunopotentiator which characteristically contains
20 clove extract.

Also, the present invention provides a drug against immunosuppression which characteristically contains clove extract.

Furthermore, the present invention provides an
25 immunopotentiator which characteristically contains

Geranium herb extract.

Also, the present invention provides a drug against immunosuppression which characteristically contains Geranium herb extract.

5 Furthermore, the present invention provides an immunopotentiator which characteristically contains rosemary extract.

Also, the present invention provides a drug against immunosuppression which characteristically
10 contains rosemary extract.

BRIEF EXPLANATION OF THE DRAWING

FIG. 1 shows the reduction in antigen
15 presentation by Langerhans' cells due to UV exposure and the effect of glutathione (GSH) to prevent this reduction.

FIG. 2 shows the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in
20 Langerhans' cells due to UV irradiation and the preventive effect of Scutellaria root extract.

FIG. 3 shows the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation and the
25 preventive effect of linden extract.

FIG. 4 shows the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation and the preventive effect of clove extract.

5 FIG. 5 shows the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation and the preventive effect of Geranium herb extract.

10 FIG. 6 shows the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation and the preventive effect of rosemary extract.

THE BEST MODES OF THE EMBODIMENTS

15 The configuration of the present invention is described below.

Glutathione, which is used in the skin immunopotentiator or the drug against skin immunosuppression of the present invention, is a SH compound which exists most abundantly in a living body. It enzymatically and/or non-enzymatically reacts with the disulfides of proteins and such and has a function of maintaining the SH's. This reaction converts it to the oxidized form of
25 glutathione.

Scutellaria root extract, which is used in the skin immunopotentiator or the drug against skin immunosuppression of the present invention, is an organic solvent extract of the root of Scutellaria
5 baicalensis Georgi, a plant of the Lamiaceae family. For example, dried Scutellaria root powder or non-dried cut-up Scutellaria root is stirred in water or alcohol such as methanol, ethanol, propylene glycol and 1,3-butylene glycol for extraction while being
10 heated up to 30-70 °C for 1-10 hours or at room temperature for 1-20 days. After filtration, the filtrate is concentrated and then this concentrate is stirred with purified water to precipitate yellow powder, which is dried for use. In the present
15 invention, the Scutellaria root extract can be used at the concentrate stage or at the dry stage.

Linden extract, which is used in the immunopotentiator or the drug against immunosuppression of the present invention, is a
20 water or organic solvent extract of linden, which is a plant of the Tilia family (Tilia platyphyllos Scop., Tilia cordata Mill. and Tilia europaea). For example, dried linden powder or non-dried cut-up linden is stirred in water or alcohol such as methanol, ethanol,
25 propylene glycol and 1,3-butylene glycol for

660313 2624769
extraction while being heated up to 30-70°C for 1-10
hours or at room temperature for 1-20 days. After
filtration, the filtrate is concentrated and then dried
by vacuum concentration. In the present invention,
5 the linden extract can be used at the concentrate
stage or at the dried solid stage.

Clove extract, which is used in the
immunopotentiator or the drug against
immunosuppression of the present invention, is a
10 water or organic solvent extract of clove (*Syzygium
aromaticum* Merrill et Perry) of the Myrtaceae family.
For example, dried powder of buds, leaves, seeds, the
above-ground plant or the whole plant of clove or
non-dried sliced clove buds is stirred in water,
15 methanol, ethanol, propylene glycol, 1,3-butylene
glycol, butanol, chloroform, dichloromethane, carbon
tetrachloride, ethyl acetate, ether, etc. or a mixed
solution of these for extraction while being heated up
to 30-70°C for 1-10 hours or at room temperature for
20 1-20 days. After filtration, the filtrate is
concentrated and then dried by vacuum concentration.
In the present invention, the clove extract can be used
at the concentrate stage or at the dried solid stage.

Geranium herb extract, which is used in the
25 immunopotentiator or the drug against

immunosuppression of the present invention, is a water or organic solvent extract of *Geranium thunbergii* of the Geraniaceae family. For example, dried powder of the above-ground plant, flowers, seeds, fruits, leaves or the whole plant of *Geranium thunbergii* or non-dried sliced *Geranium thunbergii* is stirred in water, methanol, ethanol, propylene glycol, 1,3-butylene glycol, butanol, chloroform, dichloromethane, carbon tetrachloride, ethyl acetate, ether, etc. or a mixed solution of these for extraction while being heated up to 30-70°C for 1-10 hours or at room temperature for 1-20 days. After filtration, the filtrate is concentrated and then dried by vacuum concentration. In the present invention, the *Geranium* herb extract can be used at the concentrate stage or at the dried solid stage.

The blend ratio of glutathione in the immunopotentiator or the drug against immunosuppression of the present invention, as a dry weight, is 0.005-20.0 wt%, more preferably 0.01-10.0 wt%, of the total immunopotentiator or the drug against immunosuppression. A blend ratio less than 0.005 wt% would not be preferable because then the effect of the immunopotentiator or the drug against immunosuppression of the present invention would

not be sufficiently exhibited. A blend ratio more than 20 wt% would not be preferable either because then pharmaceutical preparation would become difficult. No significant increase in the effect is
5 observed when 10.0 wt% or more is blended.

The blend ratio of Scutellaria root extract, linden extract, clove extract, Geranium herb extract or rosemary extract in the immunopotentiator or the drug against immunosuppression of the present
10 invention, as a dry weight, is 0.0005-10.0 wt%, more preferably 0.001-5.0 wt%, of the total immunopotentiator or the drug against immunosuppression. A blend ratio less than 0.0005
15 wt% would not be preferable because then the effect of the immunopotentiator or the drug against immunosuppression of the present invention would not be sufficiently exhibited. A blend ratio more than 10 wt% would not be preferable either because then pharmaceutical preparation would become
20 difficult. No significant increase in the effect is observed when 5.0 wt% or more is blended.

In addition to the essential ingredient described above, the skin immunopotentiator or the drug against skin immunosuppression of the present
25 invention can contain, as necessary, those ingredients

such as are normally used in cosmetics, drugs, etc., in the form of an endermic liniment, including whitening agents, humectants, antioxidants, oil-based ingredients, ultraviolet light absorbents, anti-inflammatory agents, surfactants, thickeners, alcohols, powdered ingredients, colorings, water-based ingredients, water and various skin nutrients.

The skin immunopotentiator or the drug against skin immunosuppression of the present invention can be in any form which is conventionally used as an endermic liniment, including ointment, cream, emulsion, lotion, facial packs and bath additives. The skin immunopotentiator or the drug against skin immunosuppression of the present invention is highly useful as an immunopotentiating cosmetic or a cosmetic against skin immunosuppression.

EXAMPLES

The present invention is described in detail below by referring to examples. The present invention is not limited to these examples. The blend ratios are in weight percent units.

[1] Examples for the inventions of claims 1-4

An antigen (trinitrobenzenesulfonic acid, 1

mg/ml) was added to Langerhans' cells and, after cleaning, they were mixed and cultured with T cells obtained by purifying lymph gland cell floating fluid with a nylon fiber column (Wako). As a result, the

5 Langerhans' cells presented the antigen to the T cells and the T cells multiplied. However, when the antigen was added after irradiating the Langerhans' cells with UV and then the mixed culture with the T cells was conducted, a reduction in the multiplication

10 of the T cells was observed because the antigen presentation function of the Langerhans' cells was suppressed. We added 3 mM of glutathione (GSH) during the ultraviolet light irradiation to study the protection effect of glutathione against the

15 suppression of the antigen presentation function of the Langerhans' cells by UV. The results are shown in FIG. 1. The vertical axis of FIG. 1 shows the multiplication of the T cells. An increase in T cells indicates that the immune functions are working.

20 The horizontal axis shows whether the addition of the antigen, the UV irradiation and the addition of glutathione (GSH) were carried out or not by using "+" or "-" ("+" indicates the irradiation or the addition was carried out and "-" indicates the irradiation or

25 the addition did not take place). FIG. 1 indicates

Perfume	Appropriate amount
Ion exchanged water	Balance

(Preparation method)

5 Propylene glycol, glutathione and caustic potash
were added to ion exchanged water and dissolved,
then heated up to and maintained at 70°C (water
phase). The other ingredients were mixed and heat-
melted and then the temperature was maintained at
10 70°C (oil phase). The oil phase was gradually added
to the water phase and, after all was added, the
temperature was maintained at the same temperature
to allow the reaction to occur. Finally, the product
was homogeneously emulsified using a homogenizer
15 and cooled to 30°C while being thoroughly stirred.

"Example 2 Cream"

(Recipe)

	Stearic acid	2.0 wt%
20	Stearyl alcohol	7.0
	Lanolin hydrate	2.0
	Squalane	5.0
	2-octyldodecyl alcohol	6.0
	Polyoxyethylene (25 moles) cetyl alcohol ether	
25		3.0

	Glycerine monostearic ester	2.0
	Propylene glycol	5.0
	Glutathione	0.05
	Ethyl paraben	0.3
5	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

Propylene glycol was added to ion exchanged
 10 water and heated up to and maintained at 70°C (water
 phase). The other ingredients were mixed and heat-
 melted and then the temperature was maintained at
 70°C (oil phase). The oil phase was added to the
 water phase and, after pre-emulsification, the
 15 product was homogeneously emulsified using a
 homogenizer and cooled to 30 °C while being
 thoroughly stirred.

"Example 3 Cream"

20 (Recipe)

	Solid paraffin	5.0	wt%
	Beeswax	10.0	
	Vaseline	15.0	
	Liquid paraffin	41.0	
25	Glycerine monostearic ester	2.0	

Polyoxyethylene (20 moles) sorbitan monolauric ester

2.0

Soap powder

0.1

Borax

0.2

5 Glutathione

0.05

Ascorbic acid

2.0

Ethyl paraben

0.3

Perfume

Appropriate amount

Ion exchanged water

Balance

10

(Preparation method)

Soap powder and borax were added to ion exchanged water and dissolved, heated up to and maintained at 70 °C (water phase). The other

15

ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase).

The oil phase was gradually added to the water phase while being stirred to initiate the reaction. After the completion of the reaction, the product was

20

homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

"Example 4 Emulsion"

(Recipe)

25

Stearic acid

2.5 wt%

	Cetyl alcohol	1.5
	Vaseline	5.0
	Liquid paraffin	10.0
	Polyoxyethylene (10 moles) monooleic ester	
5		2.0
	Polyethylene glycol 1500	3.0
	Triethanolamine	1.0
	Carboxyvinyl polymer (product name: Carbopol 941 from B. F. Goodrich Chemical company)	
10		0.05
	Glutathione	0.01
	Octyl paradimethylaminobenzoate	1.0
	Sodium hydrogensulfite	0.01
	Arbutin	3.5
15	Ethyl paraben	0.3
	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

20 The carboxyvinyl polymer was dissolved in a small amount of ion exchanged water (A phase). Polyethylene glycol 1500 and triethanolamine were added to the rest of the ion exchanged water and heated and dissolved, after which the temperature

25 was maintained at 70°C (water phase). The other

ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the A phase was added. The product was then homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

"Example 5 Emulsion"

10 (Recipe)

Microcrystalline wax	1.0	wt%
Beeswax	2.0	
Lanolin	20.0	
Liquid paraffin	10.0	
15 Octyl paramethylaminobenzoate	3.0	
Squalane	5.0	
Sorbitan sesquioleic ester	4.0	
Polyoxyethylene (20 moles) sorbitan monooleic ester	1.0	
20 Propylene glycol	7.0	
Glutathione	10.0	
Magnesium ascorbate phosphate	3.0	
Ethyl paraben	0.3	
Perfume	Appropriate amount	
25 Ion exchanged water	Balance	

(Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the water phase and homogeneously emulsified using a homogenizer. After emulsification, the product was cooled to 30°C while being thoroughly stirred.

"Example 6 Jelly"

(Recipe)

	95% ethyl alcohol	10.0	wt%
15	Dipropylene glycol	15.0	
	Polyoxyethylene (50 moles) oleyl alcohol ether	2.0	
	Carboxyvinyl polymer (product name: Carbopol 940 from B. F. Goodrich Chemical company)	1.0	
20	Caustic soda	0.15	
	L-arginine	0.1	
	Isopropyl paramethoxycinnamate	0.1	
	Titanium oxide	5.0	
	Glutathione	7.0	
25	Sodium 2-hydroxy-4-methoxybenzophenonesulfonate		

		0.05
	Ethylenediamine-tetraacetic acid trisodium dihydrate	
		0.05
	Methyl paraben	0.2
5	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

Carbopol 940 was homogeneously dissolved in
 10 ion exchanged water. Glutathione and
 polyoxyethylene (50 moles) oleyl alcohol ether were
 dissolved in 95% ethanol and added to the water phase.
 The other ingredients were added and the mixture was
 neutralized and thickened by caustic soda and/or L-
 15 arginine.

"Example 7 Essence"

(Recipe)

(A phase)

20	Ethyl alcohol (95%)	10.0	wt%
	Polyoxyethylene (20 moles) octyldodecanol		
		1.0	
	Pantothenyl ethyl ether	0.1	
	Glutathione	1.5	
25	Methyl paraben	0.15	

(B phase)

Potassium hydroxide 0.1

(C phase)

Glycerine 5.0

5 Dipropylene glycol 10.0

Carboxyvinyl polymer (product name: Carbopol 940
from B. F. Goodrich Chemical company)

0.2

Purified water Balance

10

(Preparation method)

The A phase and C phase were, separately, each
homogeneously dissolved. The A phase was then
added to the C phase and solubilized. Finally, the B
phase was added and a container was filled with the
product.

15

"Example 8 Facial pack"

(Recipe)

20 (A phase)

Dipropylene glycol 5.0 wt%

Polyoxyethylene (60 moles) hydrogenated castor oil

5.0

(B phase)

25 Glutathione 0.01

Olive oil	5.0
Tocopherol acetate	0.2
Ethyl paraben	0.2
Perfume	0.2

5 (C phase)

Polyvinyl alcohol (degree of saponification: 90, degree of polymerization: 2,000)	13.0
Ethanol	7.0
Purified water	Balance

10

(Preparation method)

Each of the A phase, B phase and C phase was homogeneously dissolved. The B phase was added to the A phase and solubilized. The C phase was then added and a container was filled with the product.

15

"Example 9 Solid foundation"

(Recipe)

Talc	43.1	wt%
20 Kaolin	15.0	
Sericite	10.0	
Zinc flower	7.0	
Titanium dioxide	3.8	
Yellow iron oxide	2.9	
25 Black iron oxide	0.2	

	Squalane	8.0
	Isostearic acid	4.0
	POE sorbitan monooleate	3.0
	Isocetyl octanoate	2.0
5	Glutathione	1.0
	Preservative	Appropriate amount
	Perfume	Appropriate amount

(Preparation method)

- 10 The powder ingredients, from talc to black iron
oxide as listed above, were thoroughly mixed with a
blender. The oil ingredients, from squalane to
isocetyl octanoate as listed above, as well as
glutathione, the preservative and the perfume, were
15 added and, after thorough kneading, a container was
filled with the product.

"Example 10 Emulsified foundation (cream type)"

(Recipe)

20 (Powder portion)

	Titanium dioxide	10.3 wt%
	Sericite	5.4
	Kaolin	3.0
	Yellow iron oxide	0.8
25	Red iron oxide	0.3

Black iron oxide 0.2

(Oil phase)

Decamethylcyclopentasiloxane 11.5

Liquid paraffin 4.5

5 Polyoxyethylene modified dimethyl polysiloxane 4.0

(Water phase)

Purified water 50.0

1,3-butylene glycol 4.5

10 Glutathione 1.5

Ascorbyl glucoside 1.0

Sorbitan sesquioleic ester 3.0

Preservative Appropriate amount

Perfume Appropriate amount

15

(Preparation method)

After heating and stirring the water phase, the powder portion was added to it and the mixture was treated with a homogenizer. The oil phase, heated and mixed, was then added and the resulting mixture was treated with a homogenizer. The perfume was then added while stirring and the product was cooled down to room temperature.

25 [2] Examples for the inventions of claims 5-6

The immunopotentiating action and the effect of alleviating/preventing ultraviolet light-induced immunosuppression of *Scutellaria* root extract were investigated by observing the prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.

"*Scutellaria* root extract"

The *Scutellaria* root extract used in the following examples was prepared by adding water to thinly sliced skinned root of *Scutellaria baicalensis* Georgi, raising the temperature up to 50°C, adding ethanol, carrying out extraction for five hours, filtering and removing the solvent from the filtrate to obtain a concentrate.

[Testing methods and results: Prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.]

Langerhans' cells prepared by treating human skin epidermis with 0.5% trypsin was irradiated with UVA (5 J/cm², BLB lamp) and then cultured in a CO₂

incubator, with RPMI1640/10%FBS, for 24 hours at 37 °C . After the culture process, the cells were treated with the anti-MHC class II antibody labeled with FITC (from PharMingen) and the anti-ICAM-1 antibody labeled with PE (from PharMingen). A flow cytometer (XL from Epix) was used to analyse 3 x 10⁴ of the cells to measure the ICAM-1 expression. The result is shown in FIG. 2. The vertical axis of FIG. 2 shows the ICAM-1 expression ratio (%) and the horizontal axis shows the presence or absence of the Scutellaria root extract (final concentration in wt% unit). FIG. 2 indicates that the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation is prevented by the addition of the Scutellaria root extract.

Examples of using Scutellaria root extract as an immunopotentiator or a drug against immunosuppression are described below.

"Example 1 Cream"

(Recipe)

Stearic acid	5.0	wt%
Stearyl alcohol	4.0	
Isopropylmyristate	18.0	

	Glycerine monostearic ester	3.0
	Propylene glycol	10.0
	Scutellaria root extract	0.01
	Paraaminobenzoic acid	0.5
5	Caustic potash	0.2
	2-ethylhexylparamethoxycinnamic acid	
		3.0
	Preservative	Appropriate amount
	Perfume	Appropriate amount
10	Ion exchanged water	Balance

(Preparation method)

Propylene glycol, Scutellaria root extract and caustic potash were added to ion exchanged water and dissolved, then heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was gradually added to the water phase and, after all was added, the temperature was maintained at the same temperature to allow the reaction to occur. Finally, the product was homogeneously emulsified using a homogenizer and cooled to 30°C while being thoroughly stirred.

"Example 2 Cream"

(Recipe)

	Stearic acid	2.0	wt%
	Stearyl alcohol	7.0	
	Lanolin hydrate	2.0	
5	Squalane	5.0	
	2-octyldodecyl alcohol	6.0	
	Polyoxyethylene (25 moles) cetyl alcohol ether	3.0	
	Glycerine monostearic ester	2.0	
10	Propylene glycol	5.0	
	2-ethylhexylparamethoxycinnamic acid	10.0	
	Scutellaria root extract	0.05	
	Ethyl paraben	0.3	
15	Perfume	Appropriate amount	
	Ion exchanged water	Balance	

(Preparation method)

Propylene glycol was added to ion exchanged water
20 and heated up to and maintained at 70°C (water
phase). The other ingredients were mixed and heat-
melted and then the temperature was maintained at
70°C (oil phase). The oil phase was added to the
water phase and, after pre-emulsification, the
25 product was homogeneously emulsified using a

homogenizer and cooled to 30 °C while being thoroughly stirred.

"Example 3 Cream"

5 (Recipe)

Solid paraffin	5.0	wt%
Beeswax	10.0	
Vaseline	15.0	
Liquid paraffin	41.0	
10 Glycerine monostearic ester	2.0	
Polyoxyethylene (20 moles) sorbitan monolauric ester	2.0	
Soap powder	0.1	
2-ethylhexylparamethoxycinnamic acid	3.0	
15 Borax	0.2	
Scutellaria root extract	0.05	
Ascorbic acid	2.0	
Ethyl paraben	0.3	
20 Perfume	Appropriate amount	
Ion exchanged water	Balance	

(Preparation method)

25 Soap powder and borax were added to ion exchanged water and dissolved, heated up to and

maintained at 70 °C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase). The oil phase was gradually added to the water phase while being stirred to initiate the reaction. After the completion of the reaction, the product was homogeneously emulsified using a homogenizer and cooled to 30°C while being thoroughly stirred.

10 "Example 4 Emulsion"

(Recipe)

Stearic acid	2.5	wt%
--------------	-----	-----

Cetyl alcohol	1.5	
---------------	-----	--

Vaseline	5.0	
----------	-----	--

15 Liquid paraffin	10.0	
--------------------	------	--

Polyoxyethylene (10 moles) monooleic ester		
--	--	--

	2.0	
--	-----	--

Polyethylene glycol 1500	3.0	
--------------------------	-----	--

Triethanolamine	1.0	
-----------------	-----	--

20 Carboxyvinyl polymer (product name: Carbopol 941 from B. F. Goodrich Chemical company)	0.05	
---	------	--

Scutellaria root extract	0.01	
--------------------------	------	--

Octyl paradimethylaminobenzoate	1.0	
---------------------------------	-----	--

Sodium hydrogensulfite	0.01	
------------------------	------	--

25 Arbutin	3.5	
------------	-----	--

Ethyl paraben	0.3
Perfume	Appropriate amount
Ion exchanged water	Balance

5 (Preparation method)

The carboxyvinyl polymer was dissolved in a small amount of ion exchanged water (A phase). Polyethylene glycol 1500 and triethanolamine were added to the rest of the ion exchanged water and heated and dissolved, after which the temperature was maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the A phase was added. The product was then homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

20 "Example 5 Emulsion"

(Recipe)

Microcrystalline wax	1.0	wt%
Beeswax	2.0	
Lanolin	20.0	
25 Liquid paraffin	10.0	

	Octyl paramethylaminobenzoate	3.0
	2-ethylhexylparamethoxycinnamic acid	
		4.0
	Squalane	5.0
5	Sorbitan sesquioleic ester	4.0
	Polyoxyethylene (20 moles) sorbitan monooleic ester	
		1.0
	Propylene glycol	7.0
	Scutellaria root extract	10.0
10	Magnesium ascorbate phosphate	3.0
	Ethyl paraben	0.3
	Perfume	Appropriate amount
	Ion exchanged water	Balance

15 (Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the water phase and homogeneously emulsified using a homogenizer. After emulsification, the product was cooled to 30°C while being thoroughly stirred.

25 "Example 6 Jelly"

(Recipe)

95% ethyl alcohol 10.0 wt%

Dipropylene glycol 15.0

Polyoxyethylene (50 moles) oleyl alcohol ether

5 2.0

Carboxyvinyl polymer (product name: Carbopol 940
from B. F. Goodrich Chemical company) 1.0

Caustic soda 0.15

L-arginine 0.1

10 Isopropyl paramethoxycinnamate 0.1

Titanium oxide 5.0

Scutellaria root extract 7.0

Sodium 2-hydroxy-4-methoxybenzophenonesulfonate
0.05

15 Ethylenediamine-tetraacetic acid trisodium dihydrate
0.05

Methyl paraben 0.2

Perfume Appropriate amount

Ion exchanged water Balance

20

(Preparation method)

Carbopol 940 was homogeneously dissolved in
ion exchanged water. Scutellaria root extract and
polyoxyethylene (50 moles) oleyl alcohol ether were

25 dissolved in 95% ethanol and added to the water phase.

The other ingredients were added and the mixture was neutralized and thickened by caustic soda and/or L-arginine.

5 "Example 7 Essence"

(Recipe)

(A phase)

Ethyl alcohol (95%) 10.0 wt%

Polyoxyethylene (20 moles) octyldodecanol

10 1.0

Pantothenyl ethyl ether 0.1

Scutellaria root extract 1.5

Methyl paraben 0.15

(B phase)

15 Potassium hydroxide 0.1

(C phase)

Glycerine 5.0

Dipropylene glycol 10.0

Carboxyvinyl polymer (product name: Carbopol 940

20 from B. F. Goodrich Chemical company) 0.2

Purified water Balance

(Preparation method)

The A phase and C phase were, separately, each
25 homogeneously dissolved. The A phase was then

added to the C phase and solubilized. Finally, the B phase was added and a container was filled with the product.

5 "Example 8 Facial pack"

(Recipe)

(A phase)

Dipropylene glycol 5.0 wt%

Polyoxyethylene (60 moles) hydrogenated castor oil

10 5.0

(B phase)

Scutellaria root extract 0.01

Olive oil 5.0

Tocopherol acetate 0.2

15 Ethyl paraben 0.2

Perfume 0.2

(C phase)

Polyvinyl alcohol (degree of saponification: 90, degree of polymerization: 2,000) 13.0

20 Ethanol 7.0

Purified water Balance

(Preparation method)

Each of the A phase, B phase and C phase was
25 homogeneously dissolved. The B phase was added to

the A phase and solubilized. The C phase was then added and a container was filled with the product.

"Example 9 Solid foundation"

5 (Recipe)

Talc	43.1 wt%
Kaolin	15.0
Sericite	10.0
Zinc flower	7.0
10 Titanium dioxide	3.8
Yellow iron oxide	2.9
Black iron oxide	0.2
Squalane	8.0
Isostearic acid	4.0
15 POE sorbitan monooleate	3.0
Isocetyl octanoate	2.0
Scutellaria root extract	1.0
Preservative	Appropriate amount
Perfume	Appropriate amount

20

(Preparation method)

The powder ingredients, from talc to black iron oxide as listed above, were thoroughly mixed with a blender. The oil ingredients, from squalane to
25 isocetyl octanoate as listed above, as well as

Scutellaria root extract, the preservative and the perfume, were added and, after thorough kneading, a container was filled with the product.

5	"Example 10 Emulsified foundation (cream type)"		
	(Recipe)		
	(Powder portion)		
	Titanium dioxide	10.3	wt%
	Sericite	5.4	
10	Kaolin	3.0	
	Yellow iron oxide	0.8	
	Red iron oxide	0.3	
	Black iron oxide	0.2	
	(Oil phase)		
15	Decamethylcyclopentasiloxane	11.5	
	Liquid paraffin	4.5	
	Polyoxyethylene modified dimethyl polysiloxane	4.0	
	(Water phase)		
20	Purified water	50.0	
	1,3-butylene glycol	4.5	
	Scutellaria root extract	1.5	
	Ascorbyl glucoside	1.0	
	Sorbitan sesquioleic ester	3.0	
25	Preservative	Appropriate amount	

Perfume

Appropriate amount

(Preparation method)

After heating and stirring the water phase, the
5 powder portion was added to it and the mixture was
treated with a homogenizer. The oil phase, heated
and mixed, was then added and the resulting mixture
was treated with a homogenizer. The perfume was
then added while stirring and the product was cooled
10 down to room temperature.

[3] Examples for the inventions of claims 7-8

The immunopotentiating action and the effect of
alleviating/preventing ultraviolet light-induced
15 immunosuppression of linden extract were
investigated by observing the prevention against the
suppression of expression of the intercellular
adhesive molecules-1 (ICAM-1) in Langerhans' cells
due to UV irradiation.

"Linden extract"

The linden extract used in the following
examples was prepared by five-hour extraction of
thinly sliced flowers and leaves of *Tilia cordata* mill.
25 in 50% ethanol at 50°C, followed by filtering and

removal of the solvent from the filtrate to obtain a concentrate.

[Testing methods and results: Prevention against
5 the suppression of expression of the intercellular
adhesive molecules-1 (ICAM-1) in Langerhans' cells
due to UV irradiation.]

Langerhans' cells prepared by treating human
10 skin epidermis with 0.5% trypsin was irradiated with
UVA (5 J/cm², BLB lamp) and then cultured in a CO₂
incubator, with RPMI1640/10%FBS, for 24 hours at
37 °C . After the culture process, the cells were
treated with the anti-MHC class II antibody labeled
15 with FITC (from PharMingen) and the anti-ICAM-1
antibody labeled with PE (from PharMingen). A flow
cytometer (XL from Epix) was used to analyse 3 x 10⁴
of the cells to measure the ICAM-1 expression. The
result is shown in FIG. 3. The vertical axis of FIG. 3
20 shows the ICAM-1 expression ratio (%) and the
horizontal axis shows the presence or absence of the
linden extract (final concentration in wt% unit). FIG.
3 indicates that the suppression of expression of the
intercellular adhesive molecules-1 (ICAM-1) in
25 Langerhans' cells due to UV irradiation is prevented

by the addition of the linden extract.

Examples of using linden extract as an immunopotentiator or a drug against immunosuppression are described below.

5

"Example 1 Cream"

(Recipe)

	Stearic acid	5.0 wt%
	Stearyl alcohol	4.0
10	Isopropylmyristate	18.0
	Glycerine monostearic ester	3.0
	Propylene glycol	10.0
	Linden extract	0.01
	Paraaminobenzoic acid	0.5
15	2-ethylhexylparamethoxycinnamic acid	5.0
	Caustic potash	0.2
	Preservative	Appropriate amount
	Perfume	Appropriate amount
20	Ion exchanged water	Balance

(Preparation method)

Propylene glycol, linden extract and caustic potash were added to ion exchanged water and dissolved, then heated up to and maintained at 70°C

(water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was gradually added to the water phase and, after all was added, the temperature was maintained at the same temperature to allow the reaction to occur. Finally, the product was homogeneously emulsified using a homogenizer and cooled to 30°C while being thoroughly stirred.

10 "Example 2 Cream"

(Recipe)

Stearic acid	2.0	wt%
--------------	-----	-----

Stearyl alcohol	7.0	
-----------------	-----	--

Lanolin hydrate	2.0	
-----------------	-----	--

15 Squalane	5.0	
-------------	-----	--

2-octyldodecyl alcohol	6.0	
------------------------	-----	--

Polyoxyethylene (25 moles) cetyl alcohol ether	3.0	
--	-----	--

Glycerine monostearic ester	2.0	
-----------------------------	-----	--

20 Propylene glycol	5.0	
---------------------	-----	--

2-ethylhexylparamethoxycinnamic acid	10.0	
--------------------------------------	------	--

Linden extract	0.05	
----------------	------	--

Ethyl paraben	0.3	
---------------	-----	--

25 Perfume	Appropriate amount	
------------	--------------------	--

Ion exchanged water

Balance

(Preparation method)

Propylene glycol was added to ion exchanged
5 water and heated up to and maintained at 70°C (water
phase). The other ingredients were mixed and heat-
melted and then the temperature was maintained at
70°C (oil phase). The oil phase was added to the
water phase and, after pre-emulsification, the
10 product was homogeneously emulsified using a
homogenizer and cooled to 30 °C while being
thoroughly stirred.

"Example 3 Cream"

15 (Recipe)

Solid paraffin	5.0	wt%
Beeswax	10.0	
Vaseline	15.0	
Liquid paraffin	41.0	
20 Glycerine monostearic ester	2.0	
Polyoxyethylene (20 moles) sorbitan monolauric ester	2.0	
Soap powder	0.1	
2-ethylhexylparamethoxycinnamic acid		
25	1.0	

	Borax	0.2
	Linden extract	0.05
	Ascorbic acid	2.0
	Ethyl paraben	0.3
5	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

10 Soap powder and borax were added to ion
exchanged water and dissolved, heated up to and
maintained at 70 °C (water phase). The other
ingredients were mixed and heat-melted and then the
temperature was maintained at 70 °C (oil phase).
15 The oil phase was gradually added to the water phase
while being stirred to initiate the reaction. After
the completion of the reaction, the product was
homogeneously emulsified using a homogenizer and
cooled to 30°C while being thoroughly stirred.

20 "Example 4 Emulsion"

(Recipe)

	Stearic acid	2.5 wt%
	Cetyl alcohol	1.5
	Vaseline	5.0
25	Liquid paraffin	10.0

Polyoxyethylene (10 moles) monooleic ester

2.0

Polyethylene glycol 1500

3.0

Triethanolamine

1.0

5 Carboxyvinyl polymer (product name: Carbopol 941
from B. F. Goodrich Chemical company) 0.05

Linden extract

0.01

Octyl paradimethylaminobenzoate

1.0

Sodium hydrogensulfite

0.01

10 Arbutin

3.5

Ethyl paraben

0.3

Perfume

Appropriate amount

Ion exchanged water

Balance

15 (Preparation method)

The carboxyvinyl polymer was dissolved in a small amount of ion exchanged water (A phase). Polyethylene glycol 1500 and triethanolamine were added to the rest of the ion exchanged water and heated and dissolved, after which the temperature was maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the A phase was added. The

product was then homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

5 "Example 5 Emulsion"

(Recipe)

	Microcrystalline wax	1.0	wt%
	Beeswax	2.0	
	Lanolin	20.0	
10	Liquid paraffin	10.0	
	Octyl paramethylaminobenzoate	3.0	
	2-ethylhexylparamethoxycinnamic acid	5.0	
	Squalane	5.0	
15	Sorbitan sesquioleic ester	4.0	
	Polyoxyethylene (20 moles) sorbitan monooleic ester	1.0	
	Propylene glycol	7.0	
	Linden extract	10.0	
20	Magnesium ascorbate phosphate	3.0	
	Ethyl paraben	0.3	
	Perfume	Appropriate amount	
	Ion exchanged water	Balance	

25 (Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 5 70°C (oil phase). The oil phase was added to the water phase and homogeneously emulsified using a homogenizer. After emulsification, the product was cooled to 30°C while being thoroughly stirred.

10 "Example 6 Jelly"

(Recipe)

95% ethyl alcohol 10.0 wt%

Dipropylene glycol 15.0

Polyoxyethylene (50 moles) oleyl alcohol ether

15 2.0

Carboxyvinyl polymer (product name: Carbopol 940 from B. F. Goodrich Chemical company) 1.0

Caustic soda 0.15

L-arginine 0.1

20 Isopropyl paramethoxycinnamate 0.1

2-ethylhexylparamethoxycinnamic acid 0.5

Titanium oxide 5.0

Linden extract 7.0

25 Sodium 2-hydroxy-4-methoxybenzophenonesulfonate

		0.05
	Ethylenediamine-tetraacetic acid trisodium dihydrate	
		0.05
	Methyl paraben	0.2
5	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

10 Carbopol 940 was homogeneously dissolved in ion exchanged water. Linden extract and polyoxyethylene (50 moles) oleyl alcohol ether were dissolved in 95% ethanol and added to the water phase. The other ingredients were added and the mixture was neutralized and thickened by caustic soda and/or L-
15 arginine.

"Example 7 Essence"

(Recipe)

(A phase)

20	Ethyl alcohol (95%)	10.0 wt%
	Polyoxyethylene (20 moles) octyldodecanol	
		1.0
	Pantothenyl ethyl ether	0.1
	Linden extract	1.5
25	Methyl paraben	0.15

(B phase)

Potassium hydroxide 0.1

(C phase)

Glycerine 5.0

5 Dipropylene glycol 10.0

Carboxyvinyl polymer (product name: Carbopol 940
from B. F. Goodrich Chemical company) 0.2

Purified water Balance

10 (Preparation method)

The A phase and C phase were, separately, each
homogeneously dissolved. The A phase was then
added to the C phase and solubilized. Finally, the B
phase was added and a container was filled with the
product.

"Example 8 Facial pack"

(Recipe)

(A phase)

20 Dipropylene glycol 5.0 wt%

Polyoxyethylene (60 moles) hydrogenated castor oil
5.0

(B phase)

Linden extract 0.01

25 Olive oil 5.0

Tocopherol acetate	0.2
Ethyl paraben	0.2
Perfume	0.2
(C phase)	
5 Polyvinyl alcohol (degree of saponification: 90, degree of polymerization: 2,000)	13.0
Ethanol	7.0
Purified water	Balance

10 (Preparation method)

Each of the A phase, B phase and C phase was homogeneously dissolved. The B phase was added to the A phase and solubilized. The C phase was then added and a container was filled with the product.

15

"Example 9 Solid foundation"

(Recipe)

Talc	43.1 wt%
Kaolin	15.0
20 Sericite	10.0
Zinc flower	7.0
Titanium dioxide	3.8
Yellow iron oxide	2.9
Black iron oxide	0.2
25 Squalane	8.0

	Isostearic acid	4.0
	POE sorbitan monooleate	3.0
	Isocetyl octanoate	2.0
	Linden extract	1.0
5	Preservative	Appropriate amount
	Perfume	Appropriate amount

(Preparation method)

10 The powder ingredients, from talc to black iron
oxide as listed above, were thoroughly mixed with a
blender. The oil ingredients, from squalane to
isocetyl octanoate as listed above, as well as linden
extract, the preservative and the perfume, were added
and, after thorough kneading, a container was filled
15 with the product.

"Example 10 Emulsified foundation (cream type)"

(Recipe)

(Powder portion)

20	Titanium dioxide	10.3 wt%
	Sericite	5.4
	Kaolin	3.0
	Yellow iron oxide	0.8
	Red iron oxide	0.3
25	Black iron oxide	0.2

(Oil phase)

Decamethylcyclopentasiloxane	11.5
Liquid paraffin	4.5
Polyoxyethylene modified dimethyl polysiloxane	
5	4.0

(Water phase)

Purified water	50.0
1,3-butylene glycol	4.5
Linden extract	1.5
10 Ascorbyl glucoside	1.0
Sorbitan sesquioleic ester	3.0
Preservative	Appropriate amount
Perfume	Appropriate amount

15 (Preparation method)

After heating and stirring the water phase, the powder portion was added to it and the mixture was treated with a homogenizer. The oil phase, heated and mixed, was then added and the resulting mixture was treated with a homogenizer. The perfume was then added while stirring and the product was cooled down to room temperature.

[4] Examples for the inventions of claims 9-10

25 The immunopotentiating action and the effect of

alleviating/preventing ultraviolet light-induced immunosuppression of clove extract were investigated by observing the prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.

"Clove extract"

The clove extract used in the following examples was prepared by five-hour extraction of dried buds of clove (*Syzygium aromaticum* Merrill et Perry) in 50% ethanol at 50°C, followed by filtering and removal of the solvent from the filtrate to obtain a concentrate.

[Testing methods and results: Prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.]

Langerhans' cells prepared by treating human skin epidermis with 0.5% trypsin was irradiated with UVA (5 J/cm², BLB lamp) and then cultured in a CO₂ incubator, with RPMI1640/10%FBS, for 24 hours at 37 °C. After the culture process, the cells were treated with the anti-MHC class II antibody labeled

with FITC (from PharMingen) and the anti-ICAM-1 antibody labeled with PE (from PharMingen). A flow cytometer (XL from Epix) was used to analyse 3×10^4 of the cells to measure the ICAM-1 expression. The result is shown in FIG. 4. The vertical axis of FIG. 4 shows the ICAM-1 expression ratio (%) and the horizontal axis shows the presence or absence of the clove extract (final concentration in wt% unit). FIG. 4 indicates that the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation is prevented by the addition of the clove extract.

Examples of using clove extract as an immunopotentiator or a drug against immunosuppression are described below.

"Example 1 Cream"

(Recipe)

	Stearic acid	5.0	wt%
20	Stearyl alcohol	4.0	
	Isopropylmyristate	18.0	
	Glycerine monostearic ester	3.0	
	Propylene glycol	10.0	
	Linden extract	0.01	
25	Paraaminobenzoic acid	0.5	

2-ethylhexylparamethoxycinnamic acid

5.0

Caustic potash

0.2

Preservative

Appropriate amount

5 Perfume

Appropriate amount

Ion exchanged water

Balance

(Preparation method)

Propylene glycol, linden extract and caustic
10 potash were added to ion exchanged water and
dissolved, then heated up to and maintained at 70°C
(water phase). The other ingredients were mixed and
heat-melted and then the temperature was maintained
at 70°C (oil phase). The oil phase was gradually
15 added to the water phase and, after all was added, the
temperature was maintained at the same temperature
to allow the reaction to occur. Finally, the product
was homogeneously emulsified using a homogenizer
and cooled to 30°C while being thoroughly stirred.

20

"Example 2 Cream"

(Recipe)

Stearic acid

2.0 wt%

Stearyl alcohol

7.0

25 Lanolin hydrate

2.0

	Squalane	5.0
	2-octyldodecyl alcohol	6.0
	Polyoxyethylene (25 moles) cetyl alcohol ether	3.0
5	Glycerine monostearic ester	2.0
	Propylene glycol	5.0
	2-ethylhexylparamethoxycinnamic acid	10.0
	Linden extract	0.05
10	Ethyl paraben	0.3
	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

15 Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the

20 water phase and, after pre-emulsification, the product was homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

25 "Example 3 Cream"

(Recipe)

	Solid paraffin	5.0	wt%
	Beeswax	10.0	
	Vaseline	15.0	
5	Liquid paraffin	41.0	
	Glycerine monostearic ester	2.0	
	Polyoxyethylene (20 moles) sorbitan monolauric ester	2.0	
	Soap powder	0.1	
10	2-ethylhexylparamethoxycinnamic acid	1.0	
	Borax	0.2	
	Linden extract	0.05	
	Ascorbic acid	2.0	
15	Ethyl paraben	0.3	
	Perfume	Appropriate amount	
	Ion exchanged water	Balance	

(Preparation method)

- 20 Soap powder and borax were added to ion exchanged water and dissolved, heated up to and maintained at 70 °C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase).
- 25 The oil phase was gradually added to the water phase

while being stirred to initiate the reaction. After the completion of the reaction, the product was homogeneously emulsified using a homogenizer and cooled to 30°C while being thoroughly stirred.

5

"Example 4 Emulsion"

(Recipe)

	Stearic acid	2.5	wt%
	Cetyl alcohol	1.5	
10	Vaseline	5.0	
	Liquid paraffin	10.0	
	Polyoxyethylene (10 moles) monooleic ester	2.0	
	Polyethylene glycol 1500	3.0	
15	Triethanolamine	1.0	
	Carboxyvinyl polymer (product name: Carbopol 941 from B. F. Goodrich Chemical company)	0.05	
	Linden extract	0.01	
	Octyl paradimethylaminobenzoate	1.0	
20	Arbutin	3.5	
	Ethyl paraben	0.3	
	Perfume	Appropriate amount	
	Ion exchanged water	Balance	

25 (Preparation method)

The carboxyvinyl polymer was dissolved in a small amount of ion exchanged water (A phase). Polyethylene glycol 1500 and triethanolamine were added to the rest of the ion exchanged water and heated and dissolved, after which the temperature was maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the A phase was added. The product was then homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

15 "Example 5 Emulsion"
(Recipe)

	Microcrystalline wax	1.0	wt%
	Glutathione	1.0	
	Beeswax	2.0	
20	Lanolin	20.0	
	Liquid paraffin	10.0	
	Octyl paramethylaminobenzoate	3.0	
	2-ethylhexylparamethoxycinnamic acid	5.0	
25	Squalane	5.0	

	Sorbitan sesquioleic ester	4.0
	Polyoxyethylene (20 moles) sorbitan monooleic ester	1.0
	Propylene glycol	7.0
5	Linden extract	10.0
	Magnesium ascorbate phosphate	3.0
	Ethyl paraben	0.3
	Perfume	Appropriate amount
	Ion exchanged water	Balance

10

(Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-

15 melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the water phase and homogeneously emulsified using a homogenizer. After emulsification, the product was cooled to 30°C while being thoroughly stirred.

20

"Example 6 Jelly"

(Recipe)

95% ethyl alcohol	10.0	wt%
Dipropylene glycol	15.0	

25 Polyoxyethylene (50 moles) oleyl alcohol ether

		2.0
	Carboxyvinyl polymer (product name: Carbopol 940 from B. F. Goodrich Chemical company)	1.0
	Caustic soda	0.15
5	L-arginine	0.1
	Isopropyl paramethoxycinnamate	0.1
	2-ethylhexylparamethoxycinnamic acid	0.5
	Titanium oxide	5.0
10	Linden extract	7.0
	Sodium 2-hydroxy-4-methoxybenzophenonesulfonate	0.05
	Ethylenediamine-tetraacetic acid trisodium dihydrate	0.05
15	Methyl paraben	0.2
	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

20 Carbopol 940 was homogeneously dissolved in ion exchanged water. Linden extract and polyoxyethylene (50 moles) oleyl alcohol ether were dissolved in 95% ethanol and added to the water phase. The other ingredients were added and the mixture was

25 neutralized and thickened by caustic soda and/or L-

arginine.

"Example 7 Essence"

(Recipe)

5 (A phase)

Ethyl alcohol (95%) 10.0 wt%

Polyoxyethylene (20 moles) octyldodecanol

1.0

Pantothenyl ethyl ether 0.1

10 Linden extract 1.5

Methyl paraben 0.15

(B phase)

Potassium hydroxide 0.1

(C phase)

15 Glycerine 5.0

Dipropylene glycol 10.0

Carboxyvinyl polymer (product name: Carbopol 940
from B. F. Goodrich Chemical company) 0.2

Purified water Balance

20

(Preparation method)

The A phase and C phase were, separately, each
homogeneously dissolved. The A phase was then
added to the C phase and solubilized. Finally, the B

25 phase was added and a container was filled with the

product.

"Example 8 Facial pack"

(Recipe)

5 (A phase)

Dipropylene glycol	5.0 wt%
Polyoxyethylene (60 moles) hydrogenated castor oil	5.0

(B phase)

10 Linden extract	0.01
Olive oil	5.0
Tocopherol acetate	0.2
Ethyl paraben	0.2
Perfume	0.2

15 (C phase)

Polyvinyl alcohol (degree of saponification: 90, degree of polymerization: 2,000)	13.0
Ethanol	7.0
Purified water	Balance

20

(Preparation method)

Each of the A phase, B phase and C phase was homogeneously dissolved. The B phase was added to the A phase and solubilized. The C phase was then
25 added and a container was filled with the product.

"Example 9 Solid foundation"

(Recipe)

	Talc	43.1 wt%
5	Kaolin	15.0
	Sericite	10.0
	Zinc flower	7.0
	Titanium dioxide	3.8
	Yellow iron oxide	2.9
10	Black iron oxide	0.2
	Squalane	8.0
	Isostearic acid	4.0
	POE sorbitan monooleate	3.0
	Isocetyl octanoate	2.0
15	Linden extract	1.0
	Preservative	Appropriate amount
	Perfume	Appropriate amount

(Preparation method)

- 20 The powder ingredients, from talc to black iron oxide as listed above, were thoroughly mixed with a blender. The oil ingredients, from squalane to isocetyl octanoate as listed above, as well as linden extract, the preservative and the perfume, were added
- 25 and, after thorough kneading, a container was filled

with the product.

"Example 10 Emulsified foundation (cream type)"

(Recipe)

5 (Powder portion)

Titanium dioxide 10.3 wt%

Sericite 5.4

Kaolin 3.0

Yellow iron oxide 0.8

10 Red iron oxide 0.3

Black iron oxide 0.2

(Oil phase)

Decamethylcyclopentasiloxane 11.5

Liquid paraffin 4.5

15 Polyoxyethylene modified dimethyl polysiloxane
4.0

(Water phase)

Purified water 50.0

1,3-butylene glycol 4.5

20 Linden extract 1.5

Ascorbyl glucoside 1.0

Sorbitan sesquioleic ester 3.0

Preservative Appropriate amount

Perfume Appropriate amount

25

(Preparation method)

After heating and stirring the water phase, the powder portion was added to it and the mixture was treated with a homogenizer. The oil phase, heated
5 and mixed, was then added and the resulting mixture was treated with a homogenizer. The perfume was then added while stirring and the product was cooled down to room temperature.

10 [5] Examples for the inventions of claims 11-12

The immunopotentiating action and the effect of alleviating/preventing ultraviolet light-induced immunosuppression of Geranium herb extract were investigated by observing the prevention against the
15 suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.

"Geranium herb extract"

20 The Geranium herb extract used in the following examples was prepared by five-hour extraction of the thinly sliced above-ground part of Geranium thunbergii in 50% ethanol at 50 °C , followed by filtering and removal of the solvent from the filtrate
25 to obtain a concentrate.

[Testing methods and results: Prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.]

Langerhans' cells prepared by treating human skin epidermis with 0.5% trypsin was irradiated with UVA (5 J/cm², BLB lamp) and then cultured in a CO₂ incubator, with RPMI1640/10%FBS, for 24 hours at 37 °C . After the culture process, the cells were treated with the anti-MHC class II antibody labeled with FITC (from PharMingen) and the anti-ICAM-1 antibody labeled with PE (from PharMingen). A flow cytometer (XL from Epix) was used to analyse 3 x 10⁴ of the cells to measure the ICAM-1 expression. The result is shown in FIG. 5. The vertical axis of FIG. 5 shows the ICAM-1 expression ratio (%) and the horizontal axis shows the presence or absence of the Geranium herb extract (final concentration in wt% unit). FIG. 5 indicates that the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation is prevented by the addition of the Geranium herb extract.

Examples of using Geranium herb extract as an immunopotentiator or a drug against immunosuppression are described below.

5 "Example 1 Cream"

(Recipe)

	Stearic acid	5.0 wt%
	Stearyl alcohol	4.0
	Isopropylmyristate	18.0
10	Glycerine monostearic ester	3.0
	Propylene glycol	10.0
	Geranium herb extract	0.01
	Paraaminobenzoic acid	0.5
	2-ethylhexylparamethoxycinnamic acid	
15		5.0
	Caustic potash	0.2
	Preservative	Appropriate amount
	Perfume	Appropriate amount
	Ion exchanged water	Balance

20

(Preparation method)

Propylene glycol, Geranium herb extract and caustic potash were added to ion exchanged water and dissolved, then heated up to and maintained at 70°C (water phase). The other ingredients were mixed and

heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was gradually added to the water phase and, after all was added, the temperature was maintained at the same temperature to allow the reaction to occur. Finally, the product was homogeneously emulsified using a homogenizer and cooled to 30°C while being thoroughly stirred.

"Example 2 Cream"

10 (Recipe)

Stearic acid 2.0 wt%

Stearyl alcohol 7.0

Lanolin hydrate 2.0

Squalane 5.0

15 2-octyldodecyl alcohol 6.0

Polyoxyethylene (25 moles) cetyl alcohol ether

3.0

Glycerine monostearic ester 2.0

Propylene glycol 5.0

20 2-ethylhexylparamethoxycinnamic acid

10.0

Geranium herb extract 0.05

Ethyl paraben 0.3

Perfume Appropriate amount

25 Ion exchanged water Balance

(Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the product was homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

"Example 3 Cream"

(Recipe)

15	Solid paraffin	5.0	wt%
	Beeswax	10.0	
	Vaseline	15.0	
	Liquid paraffin	41.0	
	Glycerine monostearic ester	2.0	
20	Polyoxyethylene (20 moles) sorbitan monolauric ester	2.0	
	Soap powder	0.1	
	2-ethylhexylparamethoxycinnamic acid	1.0	
25	Borax	0.2	

	Geranium herb extract	0.05
	Ascorbic acid	2.0
	Ethyl paraben	0.3
	Perfume	Appropriate amount
5	Ion exchanged water	Balance

(Preparation method)

Soap powder and borax were added to ion
exchanged water and dissolved, heated up to and
10 maintained at 70 °C (water phase). The other
ingredients were mixed and heat-melted and then the
temperature was maintained at 70 °C (oil phase).
The oil phase was gradually added to the water phase
while being stirred to initiate the reaction. After
15 the completion of the reaction, the product was
homogeneously emulsified using a homogenizer and
cooled to 30°C while being thoroughly stirred.

"Example 4 Emulsion"

20 (Recipe)

	Stearic acid	2.5	wt%
	Cetyl alcohol	1.5	
	Vaseline	5.0	
	Liquid paraffin	10.0	
25	Polyoxyethylene (10 moles) monooleic ester		

		2.0
	Polyethylene glycol 1500	3.0
	Triethanolamine	1.0
	Carboxyvinyl polymer (product name: Carbopol 941	
5	from B. F. Goodrich Chemical company)	0.05
	Geranium herb extract	0.01
	Octyl paradimethylaminobenzoate	1.0
	Sodium hydrogensulfite	0.01
	Arbutin	3.5
10	Ethyl paraben	0.3
	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

15 The carboxyvinyl polymer was dissolved in a small amount of ion exchanged water (A phase). Polyethylene glycol 1500 and triethanolamine were added to the rest of the ion exchanged water and heated and dissolved, after which the temperature

20 was maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70 °C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the A phase was added. The

25 product was then homogeneously emulsified using a

homogenizer and cooled to 30 °C while being thoroughly stirred.

"Example 5 Emulsion"

5 (Recipe)

Microcrystalline wax 1.0 wt%

Glutathione 1.0

Beeswax 2.0

Lanolin 20.0

10 Liquid paraffin 10.0

Octyl paramethylaminobenzoate 3.0

2-ethylhexylparamethoxycinnamic acid
5.0

Squalane 5.0

15 Sorbitan sesquioleic ester 4.0

Polyoxyethylene (20 moles) sorbitan monooleic ester
1.0

Propylene glycol 7.0

Geranium herb extract 10.0

20 Magnesium ascorbate phosphate 3.0

Ethyl paraben 0.3

Perfume Appropriate amount

Ion exchanged water Balance

25 (Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 5 70°C (oil phase). The oil phase was added to the water phase and homogeneously emulsified using a homogenizer. After emulsification, the product was cooled to 30°C while being thoroughly stirred.

10 "Example 6 Jelly"

(Recipe)

95% ethyl alcohol 10.0 wt%

Dipropylene glycol 15.0

Polyoxyethylene (50 moles) oleyl alcohol ether

15 2.0

Carboxyvinyl polymer (product name: Carbopol 940 from B. F. Goodrich Chemical company) 1.0

Caustic soda 0.15

L-arginine 0.1

20 Isopropyl paramethoxycinnamate 0.1

2-ethylhexylparamethoxycinnamic acid 0.5

Titanium oxide 5.0

Geranium herb extract 7.0

25 Sodium 2-hydroxy-4-methoxybenzophenonesulfonate

		0.05
	Ethylenediamine-tetraacetic acid trisodium dihydrate	
		0.05
	Methyl paraben	0.2
5	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

Carbopol 940 was homogeneously dissolved in
 10 ion exchanged water. Geranium herb extract and
 polyoxyethylene (50 moles) oleyl alcohol ether were
 dissolved in 95% ethanol and added to the water phase.
 The other ingredients were added and the mixture was
 neutralized and thickened by caustic soda and/or L-
 15 arginine.

"Example 7 Essence"

(Recipe)

(A phase)

20	Ethyl alcohol (95%)	10.0 wt%
	Polyoxyethylene (20 moles) octyldodecanol	
		1.0
	Pantothenyl ethyl ether	0.1
	Geranium herb extract	1.5
25	Methyl paraben	0.15

(B phase)

Potassium hydroxide 0.1

(C phase)

Glycerine 5.0

5 Dipropylene glycol 10.0

Carboxyvinyl polymer (product name: Carbopol 940
from B. F. Goodrich Chemical company) 0.2

Purified water Balance

10 (Preparation method)

The A phase and C phase were, separately, each
homogeneously dissolved. The A phase was then
added to the C phase and solubilized. Finally, the B
phase was added and a container was filled with the
product.

"Example 8 Facial pack"

(Recipe)

(A phase)

20 Dipropylene glycol 5.0 wt%

Polyoxyethylene (60 moles) hydrogenated castor oil
5.0

(B phase)

Geranium herb extract 0.01

25 Olive oil 5.0

Tocopherol acetate	0.2
Ethyl paraben	0.2
Perfume	0.2
(C phase)	
5 Polyvinyl alcohol (degree of saponification: 90, degree of polymerization: 2,000)	13.0
Ethanol	7.0
Purified water	Balance

10 (Preparation method)

Each of the A phase, B phase and C phase was homogeneously dissolved. The B phase was added to the A phase and solubilized. The C phase was then added and a container was filled with the product.

15

"Example 9 Solid foundation"

(Recipe)

Talc	43.1 wt%
Kaolin	15.0
20 Sericite	10.0
Zinc flower	7.0
Titanium dioxide	3.8
Yellow iron oxide	2.9
Black iron oxide	0.2
25 Squalane	8.0

	Isostearic acid	4.0
	POE sorbitan monooleate	3.0
	Isocetyl octanoate	2.0
	Geranium herb extract	1.0
5	Preservative	Appropriate amount
	Perfume	Appropriate amount

(Preparation method)

10 The powder ingredients, from talc to black iron
oxide as listed above, were thoroughly mixed with a
blender. The oil ingredients, from squalane to
isocetyl octanoate as listed above, as well as
Geranium herb extract, the preservative and the
perfume, were added and, after thorough kneading, a
15 container was filled with the product.

"Example 10 Emulsified foundation (cream type)"

(Recipe)

(Powder portion)

20	Titanium dioxide	10.3 wt%
	Sericite	5.4
	Kaolin	3.0
	Yellow iron oxide	0.8
	Red iron oxide	0.3
25	Black iron oxide	0.2

(Oil phase)

Decamethylcyclopentasiloxane	11.5
Liquid paraffin	4.5
Polyoxyethylene modified dimethyl polysiloxane	
5	4.0

(Water phase)

Purified water	50.0
1,3-butylene glycol	4.5
Geranium herb extract	1.5
10 Ascorbyl glucoside	1.0
Sorbitan sesquioleic ester	3.0
Preservative	Appropriate amount
Perfume	Appropriate amount

15 (Preparation method)

After heating and stirring the water phase, the powder portion was added to it and the mixture was treated with a homogenizer. The oil phase, heated and mixed, was then added and the resulting mixture was treated with a homogenizer. The perfume was then added while stirring and the product was cooled down to room temperature.

25 [6] Examples for the inventions of claims 13-14

The immunopotentiating action and the effect of alleviating/preventing ultraviolet light-induced immunosuppression of rosemary extract were investigated by observing the prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.

"Rosemary extract"

The rosemary extract used in the following examples was prepared by five-hour extraction of the thinly sliced flowers of roesmary in 50% ethanol at 50°C, followed by filtering and removal of the solvent from the filtrate to obtain a concentrate.

[Testing methods and results: Prevention against the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation.]

Langerhans' cells prepared by treating human skin epidermis with 0.5% trypsin was irradiated with UVA (5 J/cm², BLB lamp) and then cultured in a CO₂ incubator, with RPMI1640/10%FBS, for 24 hours at 37 °C . After the culture process, the cells were

treated with the anti-MHC class II antibody labeled with FITC (from PharMingen) and the anti-ICAM-1 antibody labeled with PE (from PharMingen). A flow cytometer (XL from Epix) was used to analyse 3×10^4 of the cells to measure the ICAM-1 expression. The result is shown in FIG. 6. The vertical axis of FIG. 6 shows the ICAM-1 expression ratio (%) and the horizontal axis shows the presence or absence of the rosemary extract (final concentration in wt% unit). FIG. 6 indicates that the suppression of expression of the intercellular adhesive molecules-1 (ICAM-1) in Langerhans' cells due to UV irradiation is prevented by the addition of the rosemary extract.

Examples of using rosemary extract as an immunopotentiator or a drug against immunosuppression are described below.

"Example 1 Cream"

(Recipe)

20	Stearic acid	5.0	wt%
	Stearyl alcohol	4.0	
	Isopropylmyristate	18.0	
	Glycerine monostearic ester	3.0	
	Propylene glycol	10.0	
25	Rosemary extract	0.01	

	Paraaminobenzoic acid	0.5
	2-ethylhexylparamethoxycinnamic acid	5.0
	Caustic potash	0.2
5	Preservative	Appropriate amount
	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

10 Propylene glycol, rosemary extract and caustic
potash were added to ion exchanged water and
dissolved, then heated up to and maintained at 70°C
(water phase). The other ingredients were mixed and
heat-melted and then the temperature was maintained
15 at 70°C (oil phase). The oil phase was gradually
added to the water phase and, after all was added, the
temperature was maintained at the same temperature
to allow the reaction to occur. Finally, the product
was homogeneously emulsified using a homogenizer
20 and cooled to 30°C while being thoroughly stirred.

"Example 2 Cream"

(Recipe)

	Stearic acid	2.0 wt%
25	Stearyl alcohol	7.0

	Lanolin hydrate	2.0
	Squalane	5.0
	2-octyldodecyl alcohol	6.0
	Polyoxyethylene (25 moles) cetyl alcohol ether	
5		3.0
	Glycerine monostearic ester	2.0
	Propylene glycol	5.0
	2-ethylhexylparamethoxycinnamic acid	
		10.0
10	Rosemary extract	0.05
	Ethyl paraben	0.3
	Perfume	Appropriate amount
	Ion exchanged water	Balance

15 (Preparation method)

Propylene glycol was added to ion exchanged water and heated up to and maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the temperature was maintained at 70°C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the product was homogeneously emulsified using a homogenizer and cooled to 30 °C while being thoroughly stirred.

25

"Example 3 Cream"

(Recipe)

	Solid paraffin	5.0	wt%
	Beeswax	10.0	
5	Vaseline	15.0	
	Liquid paraffin	41.0	
	Glycerine monostearic ester	2.0	
	Polyoxyethylene (20 moles) sorbitan monolauric ester	2.0	
10	Soap powder	0.1	
	2-ethylhexylparamethoxycinnamic acid	1.0	
	Borax	0.2	
	Rosemary extract	0.05	
15	Ascorbic acid	2.0	
	Ethyl paraben	0.3	
	Perfume	Appropriate amount	
	Ion exchanged water	Balance	

20 (Preparation method)

Soap powder and borax were added to ion
exchanged water and dissolved, heated up to and
maintained at 70 °C (water phase). The other
ingredients were mixed and heat-melted and then the
25 temperature was maintained at 70 °C (oil phase).

The oil phase was gradually added to the water phase while being stirred to initiate the reaction. After the completion of the reaction, the product was homogeneously emulsified using a homogenizer and cooled to 30°C while being thoroughly stirred.

"Example 4 Emulsion"

(Recipe)

	Stearic acid	2.5	wt%
10	Cetyl alcohol	1.5	
	Vaseline	5.0	
	Liquid paraffin	10.0	
	Polyoxyethylene (10 moles) monooleic ester	2.0	
15	Polyethylene glycol 1500	3.0	
	Triethanolamine	1.0	
	Carboxyvinyl polymer (product name: Carbopol 941 from B. F. Goodrich Chemical company)	0.05	
	Rosemary extract	0.01	
20	Octyl paradimethylaminobenzoate	1.0	
	Sodium hydrogensulfite	0.01	
	Arbutin	3.5	
	Ethyl paraben	0.3	
	Perfume	Appropriate amount	
25	Ion exchanged water	Balance	

(Preparation method)

The carboxyvinyl polymer was dissolved in a small amount of ion exchanged water (A phase).
5 Polyethylene glycol 1500 and triethanolamine were added to the rest of the ion exchanged water and heated and dissolved, after which the temperature was maintained at 70°C (water phase). The other ingredients were mixed and heat-melted and then the
10 temperature was maintained at 70 °C (oil phase). The oil phase was added to the water phase and, after pre-emulsification, the A phase was added. The product was then homogeneously emulsified using a homogenizer and cooled to 30 °C while being
15 thoroughly stirred.

"Example 5 Emulsion"

(Recipe)

	Microcrystalline wax	1.0	wt%
20	Glutathione	1.0	
	Beeswax	2.0	
	Lanolin	20.0	
	Liquid paraffin	10.0	
	Octyl paramethylaminobenzoate	3.0	
25	2-ethylhexylparamethoxycinnamic acid		

		5.0
	Squalane	5.0
	Sorbitan sesquioleic ester	4.0
	Polyoxyethylene (20 moles) sorbitan monooleic ester	
5		1.0
	Propylene glycol	7.0
	Rosemary extract	10.0
	Magnesium ascorbate phosphate	3.0
	Ethyl paraben	0.3
10	Perfume	Appropriate amount
	Ion exchanged water	Balance

(Preparation method)

Propylene glycol was added to ion exchanged
 15 water and heated up to and maintained at 70°C (water
 phase). The other ingredients were mixed and heat-
 melted and then the temperature was maintained at
 70°C (oil phase). The oil phase was added to the
 water phase and homogeneously emulsified using a
 20 homogenizer. After emulsification, the product was
 cooled to 30°C while being thoroughly stirred.

"Example 6 Jelly"

(Recipe)

25	95% ethyl alcohol	10.0 wt%
----	-------------------	----------

	Dipropylene glycol	15.0
	Polyoxyethylene (50 moles) oleyl alcohol ether	2.0
	Carboxyvinyl polymer (product name: Carbopol 940	
5	from B. F. Goodrich Chemical company)	1.0
	Caustic soda	0.15
	L-arginine	0.1
	Isopropyl paramethoxycinnamate	0.1
	2-ethylhexylparamethoxycinnamic acid	
10		0.5
	Titanium oxide	5.0
	Rosemary extract	7.0
	Sodium 2-hydroxy-4-methoxybenzophenonesulfonate	0.05
15	Ethylenediamine-tetraacetic acid trisodium dihydrate	0.05
	Methyl paraben	0.2
	Perfume	Appropriate amount
	Ion exchanged water	Balance

20

(Preparation method)

Carbopol 940 was homogeneously dissolved in ion exchanged water. Rosemary extract and polyoxyethylene (50 moles) oleyl alcohol ether were dissolved in 95% ethanol and added to the water phase.

The other ingredients were added and the mixture was neutralized and thickened by caustic soda and/or L-arginine.

5 "Example 7 Essence"

(Recipe)

(A phase)

Ethyl alcohol (95%) 10.0 wt%

Polyoxyethylene (20 moles) octyldodecanol

10 1.0

Pantothenyl ethyl ether 0.1

Rosemary extract 1.5

Methyl paraben 0.15

(B phase)

15 Potassium hydroxide 0.1

(C phase)

Glycerine 5.0

Dipropylene glycol 10.0

Carboxyvinyl polymer (product name: Carbopol 940

20 from B. F. Goodrich Chemical company) 0.2

Purified water Balance

(Preparation method)

The A phase and C phase were, separately, each
25 homogeneously dissolved. The A phase was then

added to the C phase and solubilized. Finally, the B phase was added and a container was filled with the product.

5 "Example 8 Facial pack"

(Recipe)

(A phase)

Dipropylene glycol 5.0 wt%

Polyoxyethylene (60 moles) hydrogenated castor oil

10 5.0

(B phase)

Rosemary extract 0.01

Olive oil 5.0

Tocopherol acetate 0.2

15 Ethyl paraben 0.2

Perfume 0.2

(C phase)

Polyvinyl alcohol (degree of saponification: 90, degree
of polymerization: 2,000) 13.0

20 Ethanol 7.0

Purified water Balance

(Preparation method)

Each of the A phase, B phase and C phase was
25 homogeneously dissolved. The B phase was added to

the A phase and solubilized. The C phase was then added and a container was filled with the product.

"Example 9 Solid foundation"

5 (Recipe)

Talc	43.1 wt%
Kaolin	15.0
Sericite	10.0
Zinc flower	7.0
10 Titanium dioxide	3.8
Yellow iron oxide	2.9
Black iron oxide	0.2
Squalane	8.0
Isostearic acid	4.0
15 POE sorbitan monooleate	3.0
Isocetyl octanoate	2.0
Rosemary extract	1.0
Preservative	Appropriate amount
Perfume	Appropriate amount

20

(Preparation method)

The powder ingredients, from talc to black iron oxide as listed above, were thoroughly mixed with a blender. The oil ingredients, from squalane to
25 isocetyl octanoate as listed above, as well as rosemary

extract, the preservative and the perfume, were added and, after thorough kneading, a container was filled with the product.

5 "Example 10 Emulsified foundation (cream type)"

(Recipe)

(Powder portion)

Titanium dioxide 10.3 wt%

Sericite 5.4

10 Kaolin 3.0

Yellow iron oxide 0.8

Red iron oxide 0.3

Black iron oxide 0.2

(Oil phase)

15 Decamethylcyclopentasiloxane 11.5

Liquid paraffin 4.5

Polyoxyethylene modified dimethyl polysiloxane
4.0

(Water phase)

20 Purified water 50.0

1,3-butylene glycol 4.5

Rosemary extract 1.5

Ascorbyl glucoside 1.0

Sorbitan sesquioleic ester 3.0

25 Preservative Appropriate amount

Perfume

Appropriate amount

(Preparation method)

After heating and stirring the water phase, the
5 powder portion was added to it and the mixture was
treated with a homogenizer. The oil phase, heated
and mixed, was then added and the resulting mixture
was treated with a homogenizer. The perfume was
then added while stirring and the product was cooled
10 down to room temperature.

INDUSTRIAL APPLICABILITY OF THE INVENTION

The present invention can provide a superior
skin immunopotentiator or drug against skin
15 immunosuppression which, through external
application, prevents a reduction in the skin immune
functions due to ultraviolet light.

CLAIMS

1. An immunopotentiator for preventing
ultraviolet light-induced skin immunosuppression
5 which characteristically contains glutathione.

2. A drug against ultraviolet light-induced
skin immunosuppression which characteristically
contains glutathione.

3. An immunopotentiating endermic liniment
10 for preventing ultraviolet light-induced skin
immunosuppression.

4. An endermic liniment against ultraviolet
light-induced skin immunosuppression which
characteristically contains glutathione.

5. An immunopotentiator for preventing
15 ultraviolet light-induced skin immunosuppression
which characteristically contains Scutellaria root
extract.

6. A drug against ultraviolet light-induced
20 skin immunosuppression which characteristically
contains Scutellaria root extract.

7. An immunopotentiator which
characteristically contains linden extract.

8. A drug against immunosuppression which
25 characteristically contains linden extract.

9. An immunopotentiator which characteristically contains clove extract.

10. A drug against immunosuppression which characteristically contains clove extract.

5 11. An immunopotentiator which characteristically contains Geranium herb extract.

12. A drug against immunosuppression which characteristically contains Geranium herb extract.

10 13. An immunopotentiator which characteristically contains rosemary extract.

14. A drug against immunosuppression which characteristically contains rosemary extract.

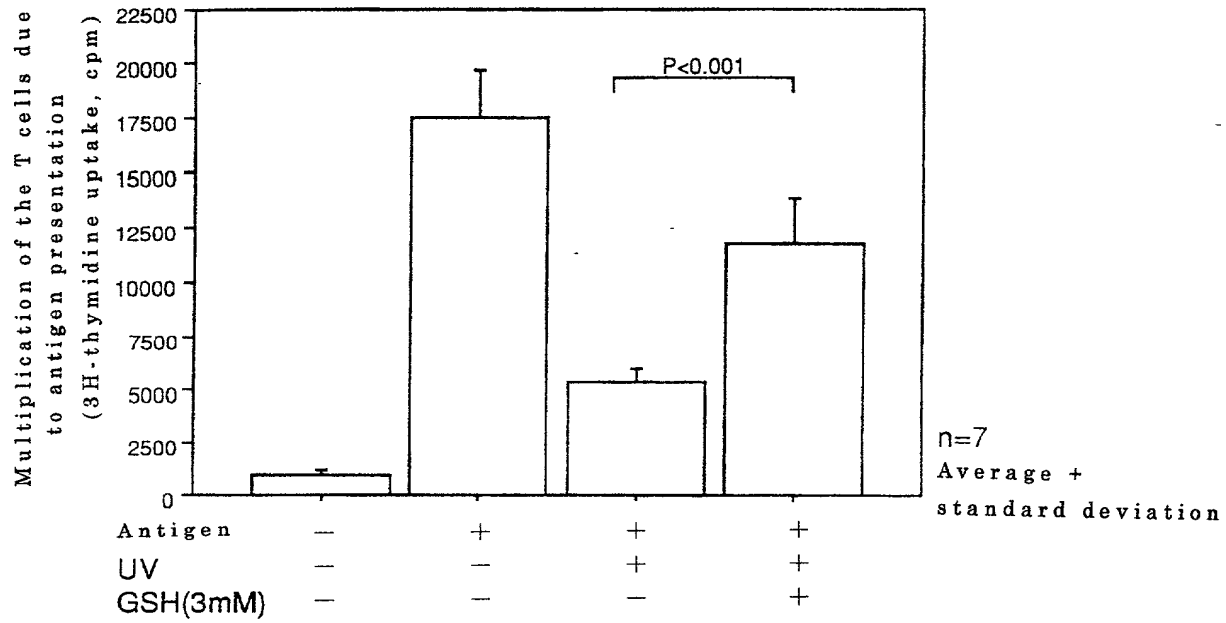
ABSTRACT

An immunopotentiator for preventing ultraviolet light-induced skin immunosuppression or
5 a drug against ultraviolet light-induced skin immunosuppression which contains glutathione or Scutellaria root extract. Also, an immunopotentiator or a drug against immunosuppression which contains linden extract,
10 clove extract, Geranium herb extract or rosemary extract. They can prevent a reduction of immune functions due to ultraviolet light.

66349 462460

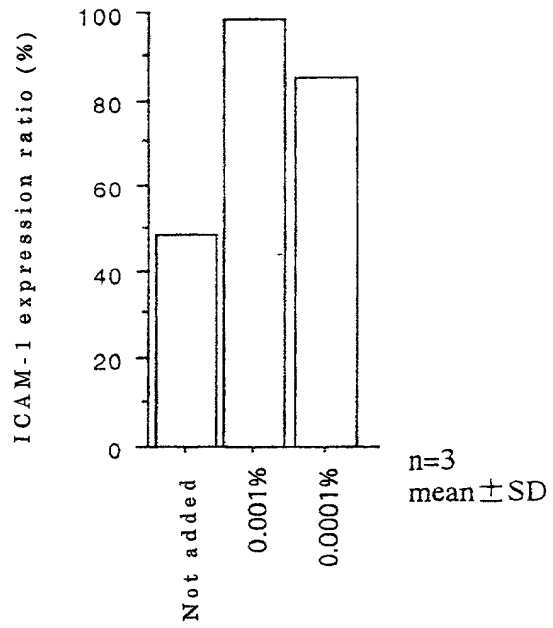
1/6

FIG. 1

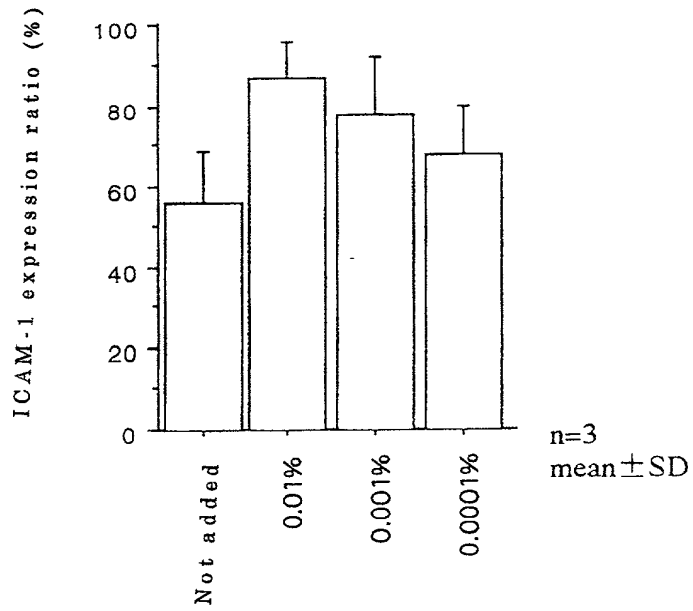


2/6

FIG. 2

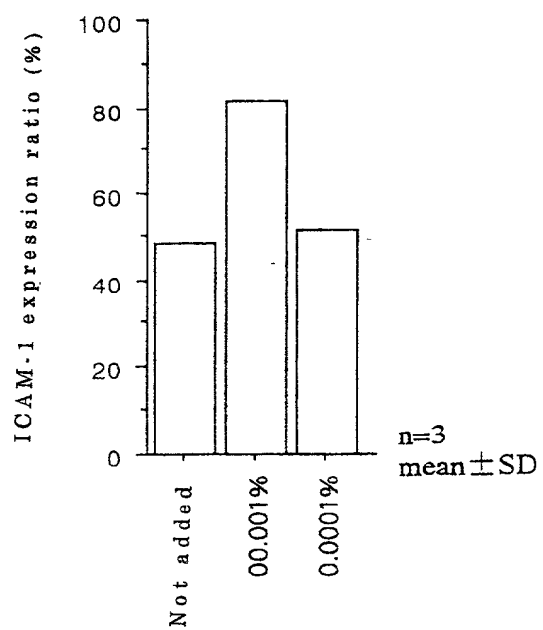


3/6
FIG. 3

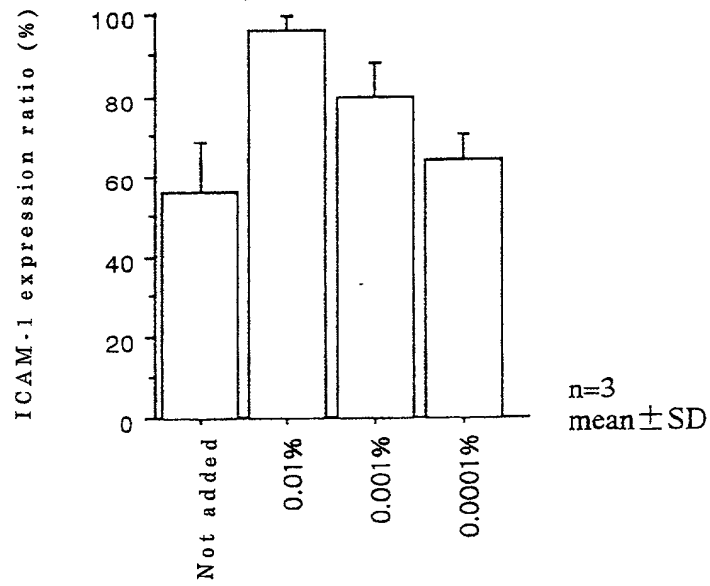


4/6

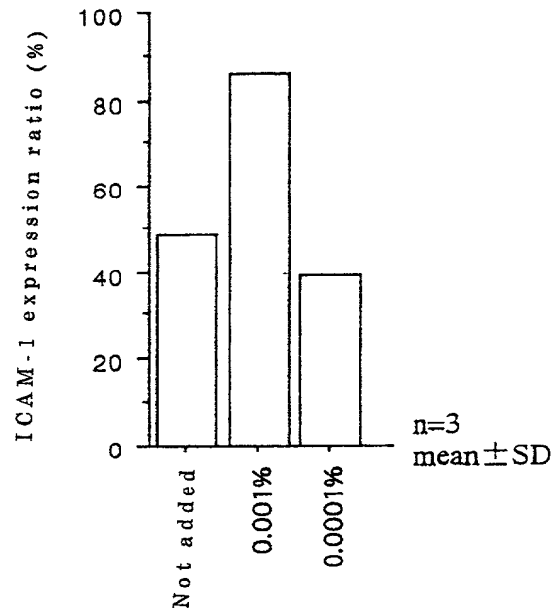
FIG. 4



5/6
FIG. 5



6/6
FIG. 6



ATTORNEY DOCKET NO: TOS-123-USA-PCT

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: IMMUNOPOTENTIATORS

the specification of which is ☐ attached and/or ☒ was filed on November 5, 1998 as Application Serial No. 09/147,237 and was amended on (if applicable)

☒ international (PCT) application No. PCT/JP98/01094 filed MAR. 16, 1998 and as amended on (if any).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

COUNTRY	APPLICATION NUMBER	DATE OF FILING	PRIORITY CLAIMED UNDER 35 U.S.C. 119
JAPAN	9-87660	MAR. 21, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
JAPAN	9-163275	JUN. 05, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
JAPAN	9-185884	JUN. 26, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
JAPAN	9-185885	JUN. 26, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
JAPAN	9-224240	AUG. 06, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
JAPAN	9-225642	AUG. 07, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
JAPAN	9-225643	AUG. 07, 1997	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION NUMBER	DATE OF FILING	STATUS (Patented, Pending, Abandoned)

I hereby appoint the following attorneys to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Law Offices of Townsend & Banta: Donald E. Townsend, Registration No. 22,069; Teresa J. Banta, Registration No. 34,543; and Donald E. Townsend, Jr., Reg. No. 43,198. Please address all correspondence to the Law Offices of Townsend & Banta, Suite 500, 1225 Eye Street, N.W., Washington, D.C. 20005

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FULL NAME OF SOLE OR FIRST INVENTOR 1-00 EIICHIRO YAGI		INVENTOR'S SIGNATURE <i>Eiichiro Yagi</i>		DATE 98-11-2
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JPX JAPAN		
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN				
FULL NAME OF SECOND JOINT INVENTOR, IF ANY 2-00 MASAKO NAGANUMA		INVENTOR'S SIGNATURE <i>Masako Naganuma</i>		DATE 98-11-4
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JPX JAPAN		
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN				

Listing of Inventors Continued on Page 2 hereof. ☒ Yes ☐ No

TURN OVER

Listing of Inventors Continued from Page 1 of Declaration and Power of Attorney for invention entitled:

IMMUNOPOTENTIATORS

FULL NAME OF THIRD JOINT INVENTOR, IF ANY ICHIRO IWAI		INVENTOR'S SIGNATURE <i>Iwai</i>	DATE 98-11-4
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF FOURTH JOINT INVENTOR, IF ANY MASATO HATAO		INVENTOR'S SIGNATURE <i>Hatao</i>	DATE Nov. 2, 1998
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF FIFTH JOINT INVENTOR, IF ANY KENJI YAMAGUCHI		INVENTOR'S SIGNATURE <i>Kenji Yamaguchi</i>	DATE 98-11-2
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF SIXTH JOINT INVENTOR, IF ANY GENJI WADA		INVENTOR'S SIGNATURE <i>Genji Wada</i>	DATE 1998-11-2
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF SEVENTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF EIGHTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF NINTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF TENTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			

ATTORNEY DOCKET NO: _____

Listing of Inventors Continued from Page 1 of Declaration and Power of Attorney for invention entitled:

IMMUNOPOTENTIATORS

FULL NAME OF THIRD JOINT INVENTOR, IF ANY 3-00 ICHIRO IWAI		INVENTOR'S SIGNATURE <i>Ichiro Iwai</i>	DATE 98-11-4
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN JPX			
FULL NAME OF FOURTH JOINT INVENTOR, IF ANY 4-00 MASATO HATAO		INVENTOR'S SIGNATURE <i>Masato Hatao</i>	DATE Nov. 2, 1998
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JPX JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF FIFTH JOINT INVENTOR, IF ANY 5-00 KENJI YAMAGUCHI		INVENTOR'S SIGNATURE <i>Kenji Yamaguchi</i>	DATE 98-11-2
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JPX JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF SIXTH JOINT INVENTOR, IF ANY 6-00 GENJI WADA		INVENTOR'S SIGNATURE <i>Genji Wada</i>	DATE 1998-11-2
RESIDENCE C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN		CITIZENSHIP JPX JAPAN	
POST OFFICE ADDRESS C/O SHISEIDO RESEARCH CENTER 1, SHISEIDO COMPANY, LTD. 1050, NIPPA-CHO, KOHOKU-KU, YOKOHAMA-SHI, KANAGAWA 223-8553 JAPAN			
FULL NAME OF SEVENTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF EIGHTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF NINTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF TENTH JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			